

**Claims**

1. A method of regulating apoptosis in a cell, said method comprising targeting an abnormally or alternatively spliced mRNA, an abnormally or alternatively structured mRNA, or a product of either.

5

2. A method according to claim 1 further comprising targeting the junctions of the mRNA molecule that is abnormally spliced or abnormally structured.

3. A method according to claim 1 further comprising targeting a protein product 10 following translation of the abnormally spliced or abnormally structured mRNA.

4. A method according to any of claims 1 to 3 further comprising the selective silencing of abnormal splice variants of the Bcl-2 gene.

15 5. A method according to claim 4 further comprising the targeting of any of the abnormal splice variants selected from the group consisting of: Bcl-2 $\alpha$ -591, Bcl-2 $\alpha$ -588, Bcl-2 $\alpha$ -480, Bcl-2 $\alpha$ -633, Bcl-2 $\beta$ -489, Bcl-2 $\beta$ -474, Bcl-2 $\beta$ -420 and/or Bcl-2 $\beta$ -315.

20 6. A method according to claim 5 further comprising targeting of the mRNA sequence flanking the splice junction between nucleotides 111 and 241 of Bcl-2 $\alpha$ -591.

7. A method according to any of the preceding claims further comprising targeting an abnormally spliced mRNA or a product thereof, by introducing into a cell containing a gene which is abnormally spliced and which is to be targeted, an RNA construct having a nucleotide sequence which is homologous to mRNA within 5 said cell wherein said mRNA includes genetic information of the gene element that is abnormally spliced.

8. A method according to claim 7 wherein the RNA construct is a small interfering dsRNA (siRNA).

10

9. A method according to claim 8 wherein the siRNA is up to 28 nucleotides long.

10. A method according to any of claims 1 to 6, further comprising targeting an 15 abnormally spliced mRNA or a product thereof, by introducing into a cell containing a gene which is abnormally spliced and which is to be targeted, an agent selected from the group consisting of: small molecule or protein; polypeptide; peptide; aptamer; chemical; antibody; nucleic acid; polypeptide or nucleotide probe; anti-sense RNA; shRNA; miRNA; and Bcl-2 derived products including abnormal Bcl-2 20 splice variants which inhibit Bcl-2 either directly or indirectly, which agent interacts with or binds with the abnormally spliced mRNA or protein expressed by the abnormally spliced mRNA.

11. A nucleotide construct with a nucleotide sequence which is homologous to mRNA transcribed from an abnormally spliced gene.
12. A nucleotide construct according to claim 11 wherein said construct 5 comprises dsRNA.
13. A nucleotide construct according to claim 12 wherein the construct is 20 to 28 nucleotides long.
- 10 14. A nucleotide construct according to claim 13 wherein the RNA construct is 21 to 22 nucleotides long.
15. A nucleotide construct such as siRNA, anti-sense RNA, shRNA or miRNA as means for silencing the expression of an abnormally spliced gene for use as a 15 medicament.
16. An agent selected from the group consisting of: small molecule or protein; polypeptide; peptide; aptamer; chemical; antibody; nucleic acid; polypeptide or nucleotide probe, which agent interacts with or binds with a protein expressed by an 20 abnormally spliced mRNA for use as a medicament.
17. A nucleotide construct such as siRNA, anti-sense RNA, shRNA or miRNA for the manufacture of a medicament for the treatment of cancerous cell growth.

18. An agent selected from the group consisting of: small molecule or protein; polypeptide; peptide; aptamer; chemical; antibody; nucleic acid; polypeptide or nucleotide probe which agent interacts with or binds with a protein expressed by an abnormally spliced mRNA for the manufacture of a medicament for the treatment of 5 cancerous cell growth.

19. A pharmaceutical composition comprising a nucleotide construct such as siRNA, anti-sense RNA, shRNA or miRNA and a pharmaceutically acceptable diluent or carrier.

10

20. A pharmaceutical composition comprising an agent selected from the group consisting of: small molecule or protein; polypeptide; peptide; aptamer; chemical; antibody; nucleic acid; polypeptide or nucleotide probe which agent interacts with or binds with a protein expressed by an abnormally spliced mRNA and a 15 pharmaceutically acceptable diluent or carrier.

21. Use of a DNA or RNA expression vector as a delivery means for a molecule which is used in the targeting of an abnormally spliced mRNA or a product thereof.

20 22. A DNA or RNA expression vector comprising an expression cassette including the nucleotide sequence selected from the group consisting of;  
a) the nucleic acid sequence of the abnormally spliced gene element as shown in Fig 1;

b) a nucleic acid molecule which hybridizes to the nucleic acid sequence of  
(a);

c) a nucleic acid molecule which has a nucleic acid sequence which is  
degenerate because of the genetic code to the sequences in a) and b) and any  
sequence which is complimentary to any of the above sequences;  
5 wherein the expression cassette is transcriptionally linked to a promoter  
sequence.

10

15

20